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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,967	ALL-ERICSSON ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 5-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-2 and 5-7 are presented for examination.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's payment and submission filed May 10, 2010 was received and entered into the present application. Accordingly, prosecution has been reopened.

Claims 1-2 and 5-7 remain pending. Claim 4 is cancelled. Claims 1 and 5-7 are amended.

Applicant's arguments, filed May 10, 2010, have been fully considered. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description Requirement, New Matter (New Grounds of Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 5-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, the specification and claims as originally filed fail to provide adequate written

description for the newly added limitation directed to the administration of the methanesulfonate salt of of 4-(4-methyl piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl) pyrimidin-2-ylamino)phenyl]-benzamide in a therapeutically effective dose for promoting cell death in uveal melanoma (claim 1).

MPEP §2163 states, "The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test of sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))…Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)."

Applicant provides relevant disclosure at p.3, para.3, of the instant specification, which states: "The invention relates to a method of treating a warm-blooded animal having uveal melanoma comprising administering to said animal in need for such a treatment Compound I or a pharmaceutically acceptable salt thereof, in a quantity which is therapeutically effective against uveal melanoma."

The disclosure of the use of, specifically, an amount of Compound I or a pharmaceutically

acceptable salt thereof (which, for the record, Compound I is equivalent to the active agent 4-(4-methyl piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl) pyrimidin-2-ylamino)phenyl]-benzamide as evidenced by Applicant's disclosure at p.1 of the instant specification), such as the disclosed methanesulfonate salt, that is therapeutically effective against uveal melanoma fails to provide adequate written support to now narrow the claims to read upon an amount that is *therapeutically effective for promoting cell death in uveal melanoma*. This is a concept that is not adequately supported by the written description of the invention as provided in the specification and claims as originally filed because the specific disclosure of an amount of the compound 4-(4-methyl piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl) pyrimidin-2-ylamino)phenyl]-benzamide or a pharmaceutically acceptable salt thereof (i.e., in the instant case, the methanesulfonate salt) that is therapeutically effective against uveal melanoma does not provide adequate support to then narrow the claims to read upon the use of an amount of the same that is *therapeutically effective specifically for the purpose of promoting cell death in uveal melanoma*. This newly amended limitation represents a narrowing of the subject matter both claimed and disclosed in the specification and claims as originally filed that is not adequately supported, either explicitly or implicitly, by the original disclosure and clearly circumscribes a concept that was not in Applicant's possession at the time of the invention.

As stated in MPEP §2163, "The subject matter of the claim need not be described literally (i.e., using the same terms of *in haec verba*) in order for the disclosure to satisfy the description requirement." However, considering the teachings provided in the specification as originally filed, Applicant has failed to provide the necessary teachings, by describing the claimed invention in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of the concept of the administration of the methanesulfonate salt of 4-(4-methyl piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl) pyrimidin-2-ylamino)phenyl]-benzamide in a therapeutically effective dose for promoting cell death in uveal melanoma (claim 1).

Accordingly, the claims are considered to lack sufficient written description and are properly rejected under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description Requirement

(New Grounds of Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 5-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, the specification as originally filed fails to provide adequate written description for therapeutically effective doses for promoting cell death in uveal melanoma when administered to a mammalian subject in need of treatment (claim 1).

Applicant provides a functional description of the dose of the compound 4-(4-methyl piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl) pyrimidin-2-ylamino)phenyl]-benzamide to be administered (i.e., that it is effective to promote cell death in uveal melanoma in a mammal in need of such treatment), but has failed to provide any description of the particular amounts, or a range of amounts, that are actually functional to achieve the effect as instantly claimed and would provide adequate written description of these claimed genera of amounts capable of being therapeutically effective to promote cell death in uveal melanoma when administered to a mammal in need of such treatment that Applicant was actually in possession of, and intended to be used within the context of the present invention, at the time of the invention.

Applicant discloses at p.4, para.2, "Depending on age, individual condition, mode of administration, and the clinical picture in question, effective doses, for example daily doses of Compound I or a pharmaceutically acceptable salt thereof corresponding to 100 to 1000 mg of the free base as active moiety, especially 800 rag, are administered to warm-blooded animals of about 70 kg body weight. Preferably, the warm-blooded animal is a human. For patients with an inadequate response to daily doses, dose escalation can be safely considered and patients may be treated as long as they benefit from treatment and in the absence of limiting toxicities." Applicant provides various studies of the instantly claimed compound *in vitro* using various concentrations in four different uveal melanoma cell lines.

Though such disclosure of this range of amounts and concentrations used *in vitro* are acknowledged, it is not explicitly clear that this disclosed range of amounts, in fact, functions to achieve this instantly claimed function of promoting cell death in uveal melanoma when administered to a mammalian subject in need of treatment according to the instant claims. As a result, the instant specification appears to lack any specific description of the amounts that would fall within the instantly claimed genus of therapeutically effective amounts such that these amounts could be immediately envisaged and/or readily identified. Absent such description, one of skill in the would have to undertake extensive hit or miss testing to determine the full scope of the genus, which is clearly indicative of the fact that Applicant was, in fact, *not* in possession of the full scope of amounts effective to achieve the instantly claimed function(s). This is because Applicant cannot logically be in possession of that which he has yet to identify.

Absent any clear description of even an exemplary amount that is effective to achieve the function(s) instantly claimed, it remains that Applicant has failed to clearly define the metes and bounds of the claimed genus of therapeutically effective doses that promote cell death in uveal melanoma when administered to a mammalian subject in need of treatment. While it is duly noted that the claimed genus is limited to those amounts capable of functioning in the claimed manner, it remains that Applicant has

not appropriately defined the metes and bounds of the genus even when limited by function. The specification provides no disclosure beyond the generic disclosure of the required function that would correlate a particular amount to performance of the claimed function that would be readily identifiable to one of skill in the art. Further, Applicant has failed to establish on the record that the state of the art was sufficiently well-developed that one of ordinary skill in the art at the time of the invention would have immediately envisaged the specific amounts that would perform the claimed function(s) in the instant specification. In other words, the present specification provides no disclosure beyond the generic disclosure of the required functions that would provide a means for identifying the amounts of the claimed compound that would have been amenable for use in the present invention, absent factual evidence to the contrary. Furthermore, it has been held that a wish or plan for obtaining the invention as claimed does not provide adequate written description of the invention. Rather, a precise definition, such as by structure, formula, chemical name or physical properties or a combination thereof (or, in the instant case, disclosure of at least an exemplary amount effective to provide the effect(s) claimed), is required. Please reference, e.g., *Univ. of Rochester v. G.D. Searle & Co.,* 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004).

While it is recognized that adequate written description of a limitation is not required to be stated *in haec verba* in the specification or claims as originally filed, adequate written support for claim limitations must arise from either an explicit or implicit suggestion by the disclosure to show that such a concept as claimed was actually in possession of Applicant at the time of the invention. For the reasons provided *supra*, Applicant has failed to provide the necessary teachings, by describing the claimed invention with all of its limitations using such descriptive means that fully set forth the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of therapeutically effective doses for promoting cell death in uveal melanoma when administered to a mammalian subject in need of treatment (claim 1).

Accordingly, the claims are considered to lack sufficient written description and are properly rejected under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2 and 5-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 1 is directed to a method of treating uveal melanoma said method comprising administering to a mammal in need of such a treatment the methanesulfonate salt of 4-(4-methyl piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl) pyrimidin-2-ylamino)phenyl]-benzamide in a therapeutically effective dose for promoting cell death in uveal melanoma.

In particular, there is insufficient antecedent basis for the term “the methanesulfonate salt”, since the preceding text of the claim fails to set forth any reference to "a methanesulfonate salt" *per se*.

In addition, the phrase "therapeutically effective dose for promoting cell death in uveal melanoma" renders the function of the therapeutically effective dose indefinite because the identity of the cells intended to be affected by the dose to promote "cell death" is not clearly set forth in the claim. Specifically, the claim states that the dose is effective “for promoting cell death in uveal melanoma", but it is unclear if the cells for which cell death is promoted are uveal melanoma cells or any cells contained in a subject suffering from uveal melanoma. As a result, one of ordinary skill in the art at the time of the invention would not have been reasonably apprised of the scope of subject matter for which Applicant is presently seeking protection.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman et al. (WO 99/03854; 1999) in light of Mouriaux et al. ("Implication of Stem Cell Factor in the Proliferation of Choroidal Melanocytes", *Exp. Eye Res.*, 2001; 73:151-157), cited as evidence, in view of Ijland et al. ("Expression of Angiogenic and Immunosuppressive Factors by Uveal Melanoma Cell Lines", *Melanoma Research*, 1999; 9:445-450), each already of record, for the reasons of record set forth at p.2-5 of the previous Office Action dated December 8, 2009, of which said reasons are herein incorporated by reference.

Newly amended claim 1 remains properly included in the instant rejection because Zimmerman et al. teaches the beta-crystal form of the methanesulfonic acid addition salt of 4-(4-methyl piperazin-1-

ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl) pyrimidin-2-ylamino)phenyl]-benzamide as useful for the treatment of warm-blooded animals suffering from tumor diseases, wherein a quantity of the beta-crystal form of the methanesulfonic acid addition salt of the compound effective against the disease concerned is administered to the warm-blooded animal in need of such treatment (p.17, para.1). Zimmerman et al. further discloses that an exemplary study of an oral dose of 50 mg/kg of the disclosed compound once daily was effective to inhibit the angiogenic effect of VEGF (p.16, para.2), i.e., a "therapeutically effective dose for promoting cell death" as now claimed in instant claim 1, because the inhibition of angiogenesis would have promoted cell death by cutting off the blood supply to the tumor disease, thereby eliminating the nutrients provided to the cells and eventually resulting in their death.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that the claims are now directed to the methanesulfonate salt of the compound 4-(4-methyl piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl) pyrimidin-2-ylamino)phenyl]-benzamide, which demonstrated surprising results in the Table at p.5 of the specification in promoting *in vitro* cell death on four uveal melanoma cell lines. Applicant urges theses findings of unexpected results to rebut the *prima facie* case of obviousness.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Applicant alleges that the present invention is non-obvious over the prior art because the use of the methanesulfonate salt of 4-(4-methyl-piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl)-pyrimidin-2-ylamino)phenyl]-benzamide demonstrated an unexpected anti-proliferative effect in four uveal melanoma cell lines (OCM-1, OCM-3, UM 92-1 and mel 202) and references the data presented in the Table at p.5 of the instant specification. While such results have been carefully and closely considered, Applicant continues to neglect to address the fact that several of the concentrations of methanesulfonate salt of 4-(4-methyl-piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl)-pyrimidin-2-

ylamino)phenyl]-benzamide, in fact, demonstrated an *increase* in cell proliferation in certain uveal melanoma cell lines and/or failed to demonstrate an *unexpectedly* potent anti-proliferative effect in the cell lines studied. Furthermore, as evidenced by the data in the Table at p.5 of the specification, it appears that the dose and the amount of time that said dose of the compound is allowed to incubate with the uveal melanoma cells is clearly pertinent to achieving Applicant's allegedly unexpected anti-proliferative effect.

For example, Applicant's attention is directed to the incubation of 4-(4-methyl-piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl)-pyrimidin-2-ylamino)phenyl]-benzamide methanesulfonate salt with the uveal melanoma cell line mel 202. For each concentration studied (i.e., 0.15, 0.3, 0.6, 1.25, 2.5, 5 and 10 μM) after 24 h incubation with the claimed compound, cell viability did not decrease below 92% for the majority of samples studied (i.e., 0.15, 0.3, 0.6, 2.5 and 5 μM) and only decreased below 92% for two single samples (i.e., 1.25 μM, which had 83% viability, and 10 μM, which had 78% viability). More importantly, however, following 24 h incubation with the claimed compound in the second study, cell viability actually *increased* with select concentrations [please see, in particular, 0.3 μM (105% viability); 0.6 μM (104% viability); and 5 μM (101% viability)] and did not demonstrate a particularly potent anti-proliferative effect [please see, in particular, 0.15 μM (98% viability); 1.25 μM (95% viability); and 10 μM (87% viability)].

Incubation for 48 h clearly demonstrated a greater anti-proliferative effect over incubation for only 24 h and further supported a trend to increase the anti-proliferative effect with an increase in dose. Please see, e.g., study (1) and (2) in uveal melanoma cell line UM92-1, study (1) and (2) in uveal melanoma cell line OCM-1, and study (1) and (2) in uveal melanoma cell line OCM-3. Studies (1) and (2) in uveal melanoma cell line mel 202 generally supported this trend also, but further demonstrated a considerable amount of fluctuation among the concentrations of compound used. Most importantly, however, it is noted that, at lower concentrations of the compound, the anti-proliferative effect is not necessarily probative of unexpected anti-proliferative activity due to the fact that only 87% or 92%

viability was achieved using 0.15 μM of the compound in UM92-1 and only 98% or 73% viability was achieved using the same amount of compound in OCM-1 uveal melanoma cells. In light of this data, it is clear that (1) the incubation time over which the cells are exposed to the compound and (2) the concentration of the compound used for incubation are each essential to attaining any unexpectedly potent anti-proliferative activity, as evidenced by the fact that such an effect is not achieved using simply *any* incubation time or *any* concentration of the active compound.

Though it is noted that the proffered data does perhaps show an unexpected anti-proliferative effect in certain uveal melanoma cell lines using particular concentrations of 4-(4-methyl-piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl)-pyrimidin-2-ylamino)phenyl]-benzamide methanesulfonate salt in combination with particular incubation time(s) that would not necessarily have been expected from the prior art, it remains that the proffered results do not provide a basis for concluding that the claimed subject matter would not have been obvious because the results that support an unexpectedly potent anti-proliferative effect (1) generally employ at least 48h incubation time for the most potent effect and (2) are generally *unexpectedly* effective at higher concentrations of the active agent used *in vitro* (though this appears dependent upon the cell line to be treated), while the claims subject to this rejection encompass (1) *any* therapeutically effective amount of the claimed compound that promotes cell death when administered to a mammal (i.e., *in vivo* and notably in the absence of any required incubation time), and (2) any type of uveal melanoma. Further, it has not been argued or demonstrated on the record that the results obtained with the exemplified combinations would have been exemplary of the same or substantially similar results that would have been expected to occur over the entire scope of the claimed subject matter.

In this regard, MPEP §2144.08(II)(B) is relied upon and reads, in-part: "When considering whether proffered evidence is commensurate in scope with the claimed invention, Office personnel should not require the Applicant to show unexpected results over the entire range of properties possessed

by a chemical compound or composition. See, e.g., *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Evidence that the compound or composition possesses superior and unexpected properties in one of a spectrum of common properties can be sufficient to rebut a *prima facie* case of obviousness. Id. For example, a showing of unexpected results for a single member of a claimed subgenus, or a narrow portion of a claimed range would be sufficient to rebut a *prima facie* case of obviousness if a skilled artisan 'could ascertain a trend in the exemplified data that would allow him to reasonably extend the probative value thereof.' *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) (**Evidence of the unobviousness of a broad range can be proven by a narrower range when one skilled in the art could ascertain a trend that would allow him to reasonably extend the probative value thereof.**) But see, *In re Grasselli*, 713 F.2d at 743, 218 USPQ at 778 (Evidence of superior properties for sodium containing composition insufficient to establish the non-obviousness of broad claims for a catalyst with 'an alkali metal' where it was well known in the catalyst art that different alkali metals were not interchangeable and Applicant had shown unexpected results only for sodium containing materials); *In re Greenfield*, 571 F.2d 1185, 1189, 197 USPQ 227, 230 (CCPA 1978) (Evidence of superior properties in one species insufficient to establish the nonobviousness of a subgenus containing hundreds of compounds); *In re Lindner*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972) (one test not sufficient where there was no adequate basis for concluding the other claimed compounds would behave the same way)." (emphasis added)

Here, just as a single point in space fails to define a line, even though the results shown with certain concentrations of the methanesulfonate salt of 4-(4-methyl-piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl)-pyrimidin-2-ylamino)phenyl]-benzamide following particular incubation times appear to demonstrate an anti-proliferative effect that was both unexpected and unpredictable from the prior art, the results demonstrated for these discrete combinations would be insufficient to establish the non-obviousness of the entirety of the presently claimed combinations (i.e., any therapeutically effective

amount of 4-(4-methyl-piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl)-pyrimidin-2-ylamino)phenyl]-benzamide methanesulfonate salt that promotes cell death when administered to a mammalian subject in the absence of any particular length of incubation with the active compound, since not all doses were effective to promote cell death) absent any concrete evidence or scientifically sound reasoning as to why these other embodiments would have been reasonably expected to demonstrate the same unexpected effect, particularly with using different formulations of the active compound in distinctly different amounts and length of incubation.

Accordingly, while Applicant's data provided in the instant specification has been fully and carefully considered, it remains that Applicant has not provided sufficient evidence and/or explanation to support the allegation that an unexpected effect over the entire scope of the claimed subject matter has been demonstrated. Furthermore, even though an apparently unexpected effect has been demonstrated for some of the discrete combinations provided in the Example of the instant specification, Applicant has not provided any objective evidence, scientific reasoning or persuasive argument on the record to provide an adequate basis for concluding that such discrete combinations shown were somehow probative of the same (or at least substantially similar) unexpected effect over the entire scope of the claimed invention. In short, the evidence is, respectfully, insufficient to be supportive of nonobviousness on the grounds of an unexpected effect and not commensurate in scope with the claimed subject matter.

Applicant is reminded that should he rely upon unexpected results to patentably distinguish over the prior art, the present claims must be limited to the embodiment(s) which is (are), in fact, unexpected. Note also that Applicant is burdened with the responsibility of explaining why the evidence provided to support secondary considerations is probative of non-obviousness beyond what data is explicitly provided as unexpected. Please see MPEP §716.02(b)[R-2], particularly Section (II), which states, "[A]ppellants have the burden of explaining the data in any declaration they proffer as evidence of non-obviousness." *Ex parte Ishizaka*, 24 USPQ2d 1621, 1624 (Bd. Pat. App. & Inter. 1992). In the instant case, though the

instant data was provided in the instant specification and not a declaration, the burden is nonetheless on Applicant to explain the data provided as evidence of non-obviousness of the claimed subject matter.

Moreover, Applicant is reminded that, "The submission of objective evidence of patentability does not mandate a conclusion of patentability in and of itself. *In re Chupp*, 816 F.2d 643, 2 USPQ2d 1437 (Fed. Cir. 1987)." In view of this, and further in view of the fact that the provided evidence fails to be commensurate in scope with the claimed subject matter for the reasons *supra*, the totality of the evidence of nonobviousness fails to outweigh the evidence of obviousness as set forth *supra* when all of the evidence is considered. Accordingly, the rejection is properly maintained.

For these reasons *supra*, and those previously made of record at p.2-5 of the Office Action dated December 8, 2009, rejection of claims 1-2 and 5-7 is proper.

Conclusion

Rejection of claims 1-2 and 5-7 is proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Leslie A. Royds/
Primary Examiner, Art Unit 1614

July 7, 2010